3:00 p.m.

824FO-5 **Matrix Remodeling in Human Aortic Valve Disease**

Olivier Fondard, Delphine Detaint, Homa Adle, Bernard Iung, Jean-Paul Couetil, Ulrich Hvass, Mohamed Jarraya, Jean Gerota, Dominique Henin, Alec Vahanian, Jean-Baptiste Michel, Marie-Paule Jacob, CHU Xavier Bichat, Paris, France

Background: Aortic valve diseases are characterized by pathological remodeling of valvular tissue but the cellular and molecular effectors involved in these processes are not well known. Here, we investigated the role of matrix metalloproteinases (MMPs) MMP-2, MMP-9, MMP-3, MMP-7 and their inhibitors TIMPs (TIMP-1 and TIMP-2) in human aortic valve disease.

Methods: Pathological valves were collected during surgery, and the controls, non-cryopreserved homografts, were obtained from a human tissue bank. Valves were classified according to their pathology and divided into 3 groups : aortic stenosis (AS) (n=49), aortic regurgitation (AR) (n=24), aortic controls (n=4). Valves were studied histologically at the cellular and extracellular matrix levels. The biochemical analyses (gelatin and casein zymography, reverse zymography, ELISA and Western blot) were performed on valve extracts.

Results: Histological study showed fibrotic, inflammatory and calcified lesions in AS, and disorganization of collagen bundles and elastic fibers in AR. MMP-9 activity was significantly increased in AS compared to AR (AS : 20915 ± 2865 ; AR : 7776 ± 1786 densitometric units/µg of proteins ; p=0.001). MMP-3 activity was significantly increased in AS compared to controls and AR (AS : 9489 ± 1196 ; AR : 5611 ± 1611 ; controls : 290 ± 290 densitometric units/µg of proteins ; p<0.05). TIMP-1 was significantly increased in AS compared to controls and AR (AS : 51 ± 3 ; AR : 34 ± 4 ; controls : 11 ± 3 ng/100 µg of proteins ; p<0.001). The MMP-9/TIMP-1 ratio was significantly decreased in AS and AR compared to controls (AS : 415 ± 55 ; AR : 426 ± 215 ; controls : 2523 ± 1295 ; p<0.0001). Results obtained for MMP-2, MMP-7 and TIMP-2 were not statistically different between groups.

Conclusion: This study demonstrates the involvement of the MMP system in the extracellular matrix remodeling of both AS and AR. The increases in MMP-9 and MMP-3 clearly provide further proof of the inflammatory state of the pathological valves. These changes are more severe in AS than in AR.

3:15 p.m.

824FO-6 **Percutaneous Implantation of Prosthetic Heart Valves: From Animal Model to First Human Implantation in Calcific Aortic Stenosis**

Alain Cribier, Helene Eltchaninoff, Christophe Tron, Fabrice Bauer, Genevieve Derumeaux, Assaf Bash, Nicolas Borenstein, Charles Nicolle Hospital, Rouen, France

Background: Percutaneous implantation of prosthetic heart valve (PHV) was shown to be feasible in animal and in human for pulmonary valve replacement. We developed a new PHV made of three bovine pericardial leaflets mounted into a stainless steel balloon-expandable stent (Percutaneous Valve Technologies, USA). This PHV was first tested in animals before being implanted as the last resort procedure in a 57 y-old patient with calcific aortic stenosis in cardiogenic shock, with severe associated diseases, for whom surgery had been declined.

Methods: In animals, PHV was implanted in 51 sheep at various sites: descending aorta (n=12), native pulmonary valve (PV: n=24) or aortic valve (AoV: n=15). PHV was crimped on a 23 mm diameter expandable balloon, introduced through a 24 F sheath via the jugular vein or the carotid artery, and pushed over an extrastiff wire. PHV function was assessed by hemodynamics, angiography, 2D-and trans-esophageal echocardiography (TEE) and Doppler. For human implantation, the same technique was applied. The percutaneous antegrade trans-septal route via the right femoral vein was used due to severe peripheral artery disease (PAD). Post-procedure PHV function was assessed by left ventricle and supra-aortic angiograms and by TEE every 2 weeks during follow-up.

Results: In animals, accurate PHV delivery was obtained in all but 4 cases. Successful implantations led to satisfactory PHV function. Complications were early death (< 3h) in 6 AoV and 2 PV cases and acute (AoV: 2, PV: 3) or delayed (AoV : 2; PV; 2) PHV migration. PHV function remained normal in 21/26 sheep (AoV: 2, PV : 19) with chronic (> 2 week) follow-up. In the patient case, PHV was accurately positioned within the native valve. PHV function was excellent: gradient 5 mmHg (from 30 mmHg), valve area 1.7 cm2 (from 0.6 cm2), with mild paraprothetic aortic regurgitation and no coronary occlusion, and remained optimal during follow-up, leading to hemodynamic and clinical improvement. The patient died of non cardiac cause (complication of right leg amputation for gangrene) 4 month after PHV implantation.

Conclusions: PHV might become an important therapeutic option in selected non-operable patients with calcific aortic stenosis.

Valvular Heart Disease

POSTER SESSION

1134 Biochemical Markers in Patients With Valvular Heart Disease

Monday, March 31, 2003, 3:00 p.m.-5:00 p.m.
McCormick Place, Hall A
Presentation Hour: 3:00 p.m.-4:00 p.m.

1134-21 **Natriuretic Peptide Plasma Levels Remain Elevated Six Months After Aortic Valve Replacement for Severe Aortic Stenosis**

Ivor L. Gerber, Ralph A. Stewart, Malcolm E. Legget, Teena M. West, Renelle French, John K. French, Timothy G. Yandle, A. Mark Richards, Harvey D. White, Green Lane Hospital, Auckland, New Zealand, Cardioendocrine Research Group, Christchurch, New Zealand

Introduction: Plasma natriuretic peptide (NP) levels are increased in aortic stenosis (AS) and correlate with disease severity, but the effects of aortic valve replacement (AVR)on NPs are unknown.

Methods: Twenty-three patients with AS, mean age 72±12 years, mean aortic valve area 0.74±0.19 cm2 underwent echocardiography and measurement of brain natriuretic peptide (BNP), atrial natriuretic peptide (ANP) and N-terminal brain natriuretic peptide (N-BNP) within 24 hours pre AVR and 6 months post AVR. A tissue valve was used in 18 patients and a mechanical valve in 5 patients. Combined AVR and coronary artery bypass graft surgery was performed in 11 patients. Plasma levels of BNP, ANP and N-BNP were measured in 23 age and gender matched controls.

Results: BNP, ANP and N-BNP were higher in AS patients pre AVR compared with controls, P<0.0001 for all, and remained elevated 6 months post AVR (Table). Mean ± SD echo measures pre AVR and 6 months post AVR were: peak aortic velocity 4.6±0.7 vs 2.3±0.3 m/s, P < 0.0001, mean aortic gradient 51±16 vs 12±3 mmHg, P<0.0001, LV mass 226±59 vs 200±56 g, P=0.05, and LV fractional shortening 35±12 vs. 35±8%, P=0.82 respectively. There were no regional wall motion abnormalities 6 months post AVR.

Conclusion: Despite reductions in aortic gradients and LV mass, NP levels remain elevated 6 months post AVR. This suggests the process of remodeling of the left ventricle is incomplete.

	Control	Pre AVR	6 Months	†P	‡P
BNP	7 (5-9)	25 (9-35)	16 (10-25)	0.08	<0.0001
N-BNP	17 (11-32)	96 (42-155)	75 (44-110)	0.04	<0.0001
ANP	12 (9-14)	32 (21-43)	30 (22-37)	0.84	<0.0001

NP levels expressed as median (interquartile range) pmol/l †6 months post AVR vs. pre AVR;
‡ 6 months post AVR vs. control

1134-22 **N-Terminal Pro-BNP as a Biochemical Marker for Assessing Severity of Aortic Stenosis**

Michael W. Weber, Matthias Rau, Christian Maikowski, Eva Keil, Vesselin Mitrovic, Ruzika Maksimovic, Roland R. Brandt, Christian Hamm, Kerckhoff Heart Centre, Bad Nauheim, Germany

Background: NT-proBNP a neurohormon is secreted from the myocardium and has shown to be a sensitive and specific marker for ventricular wall stress. Aortic stenosis (AS) leads to pressure overload of the left ventricle and thus to increased wall stress. Aim of this study was to evaluate the use of NT-proBNP for grading of aortic stenosis.

Methods: 68 consecutive patients (36 male; aged 70±9,4) with aortic stenosis and 17 patients (11 male; aged 70±7,8) after (> 6 month) aortic valve replacement (AVR) were included. In all patients NT-proBNP plasma levels were measured (Elecsys, Roche diagnostics). Transaortic pressure gradient (PG mean) and aortic valve area (AVA) were assessed by transthoracic and transesophageal echocardiography.

Results: Mean pressure gradient ranged from 10 to 117 mm Hg (mean 43 mm Hg) and AVA (n = 31) from 0,45 to 1,11 cm^2 (mean 0,77 cm^2). NT-proBNP levels correlated to the degree of aortic stenosis (p < 0,01). There was a significant correlation of NT-proBNP to the mean transaortic gradient and to leftventricular mass (Rho 0,474; Rho 0,338; p < 0,01). AVA was inversly correlated (Rho = - 0,48; p < 0,01).